

**Study fails to show a connection between thimerosal and autism**

The American Academy of Pediatrics provides the following information for clinicians who may be aware of recent press surrounding an article that claims to show a correlation between thimerosal and autism.<sup>1</sup> This paper uses data from the Vaccine Adverse Event Reporting System (VAERS) inappropriately and contains numerous conceptual and scientific flaws, omissions of fact, inaccuracies, and misstatements.

The most important weakness of the article is the reliance on VAERS data to draw conclusions about adverse event associations or causality. VAERS is a passive surveillance system for reporting possible vaccine adverse events that depends on health care professionals, patients, and others to file reports. Health effects reported to VAERS as being associated with vaccines may represent true adverse events, coincidental occurrences, or mistakes in filing. Inherent limits of VAERS include incomplete reporting, lack of verification of diagnoses, and lack of data on people who were immunized and did not report problems. Data from VAERS are useful for hypothesis generation (raising questions) but should not be used for research aimed at determining whether vaccines cause certain health problems (hypothesis proving), as was done in the article by Geier and Geier. For example, VAERS worked well to quickly alert investigators to the possibility of intussusception after rotavirus immunization but could not prove the association. Proof required numerous controlled studies to document the nature and frequency of this association.

The original concern regarding thimerosal in vaccines was sparked not by any trends identified in the VAERS system after 70 years of experience with thimerosal use as a vaccine preservative but by theoretic concerns about total exposures infants might receive from all mercury sources in the environment, including vaccines. Research to date involving refined, controlled studies in large populations of patients has failed to demonstrate any association between vaccines that may have used thimerosal as a preservative and neurodevelopmental disorders including autism. The authors failed to acknowledge the inherent limitations of the VAERS database when drawing conclusions of adverse event associations contained in this report and their other publications. They are equally unclear as to how their data were generated, thus preventing accurate review of their methods and replication of their outcomes.

Other flaws in the article include the following:

- The law relating to VAERS reporting is misstated. Most VAERS-reported conditions fall into a category in which voluntary and passive, not mandatory or required, events after immunization are recorded. Only a specific set of more severe adverse events are specified as mandatory under the Vaccine Injury Table, and even then, reporting is inconsistent.
- Conclusions of the 2001 Institute of Medicine Immunization Safety Review Committee report<sup>2</sup> as to what constitutes maximal permissible dose exposures to mercury are misinterpreted, and misleading statements are made concerning federal safety guidelines for mercury exposure levels that might be expected to cause harm.

- The authors fail to depict accurately the differences between pharmacokinetics of and exposure to methylmercury (found in contaminated food) and ethylmercury (found in thimerosal) and make unsubstantiated assumptions about the risks of the route of exposure (ingested versus injected).
- Adult heart disease is included as a possible thimerosal-related condition, although heart arrest reports in very young children are used in the analysis. Heart arrest in very young children (a common term used on pediatric death certificates and often unrelated to the actual cause of death) has nothing to do with adult coronary heart disease. The authors' implication that thimerosal in vaccines is a cause of acute cardiotoxic events is unfounded in any scientific or clinical reports and represents a misuse of the terminology found in VAERS reports.
- The authors fail to reveal how thimerosal exposure was calculated—a critical omission, because much of the data required to estimate mercury exposure are not available in VAERS reports. The authors' stated estimates of exposure attributable to diphtheria, tetanus, and pertussis combination vaccines (DTaP or DTwP) do not add up. Some DTaP vaccines never contained thimerosal as a preservative, and any child may have received 1 or more DTaP doses, which would have resulted in no ethylmercury exposure.
- The authors claim to have analyzed data from biologic surveillance summaries by manufacturers, although data regarding specific manufacturers (some of which incorporated thimerosal as a preservative and some of which did not) and age and year of birth of vaccine recipients are not available in the publication cited. Data as to the number of patients receiving vaccines with thimerosal plus the number of doses of

vaccine actually received by patients versus total doses of vaccine manufactured cannot be derived from biologic surveillance summaries, making the authors' claims for baselines of actual vaccine use untenable.

- Calculations for incidence rates and relative risk, which require information (age or year of birth) that is not available from biologic surveillance data, are not shown.
- An appropriate comparison is not made between thimerosal exposure and no thimerosal exposure, which is not possible using VAERS data, because one cannot be sure whether a child received a thimerosal-containing vaccine at any point before the event for which the VAERS report was created. Depending on the manufacturer, many of the children listed in VAERS reports could have received all vaccines that were free of thimerosal.
- Statistical methodology for calculating the relative risk and correlation coefficients is not stated.
- The authors claim to have performed their own analysis of a Vaccine Safety Datalink (VSD) thimerosal screening study (reference 17 in Geier and Geier), although the raw data needed to perform an independent analysis are not available in the document cited. (Note: neither the original preliminary VSD study of thimerosal and neurodevelopmental disorders nor any of the follow-up expanded studies identified a "signal" indicating any association between thimerosal and autism.)
- The authors claim that data for thimerosal exposure and autism risk follow an exponential distribution, although none of the thimerosal exposure categories had a significantly increased risk of autism. The figures used are confusing and not supported by an adequate explanation as to how they were constructed. Comparing

the occurrence of late onset, chronic conditions like autism by using acute vaccine reactions like fever, pain, and vomiting (presumably attributable to other vaccine components) as controls makes no sense as a measure of relative adverse event rates.

- When comparing early (1984-1985) to late (1990-1994) birth cohorts, the authors make arbitrary and unlikely assumptions of possible thimerosal exposure for both groups that are contrary to when thimerosal vaccines were introduced and what their expected pattern of use in the private and public sector was. The average level of thimerosal exposure claimed by the authors is not realistic.
- The authors claim high correlation coefficients for thimerosal with certain neurologic disabilities without describing the statistical methods used, which makes the results highly unreliable.
- The authors fail to note that a recently published review by Nelson and Bauman<sup>3</sup> casts doubt on the biologic plausibility of symptom similarities between mercury poisoning and autism.
- The authors claim falsely that children in the United States in 2003 may be exposed to higher levels of mercury from thimerosal contained in childhood immunizations than any time in the past, when in fact, all routinely recommended infant vaccines currently sold in the United States are free of thimerosal as a preservative and have been for more than 2 years ([www.fda.gov/cber/vaccine/thimerosal.htm#1](http://www.fda.gov/cber/vaccine/thimerosal.htm#1)).

No scientific data link thimerosal used as a preservative in vaccines with any pediatric neurologic disorder, including autism. Despite this, the Centers for Disease Control and Prevention, American Academy of Pediatrics, National Institutes of Health, and US

Public Health Service have continued to investigate this issue to put theoretic concerns about this mercury-containing compound to rest. Thimerosal continues to be used widely as a vaccine preservative in many other parts of the world where economics and sanitation concerns mandate an effective means to safeguard vaccines from contamination when stored in bulk in multidose vials. Any scientific article that can prove a thimerosal link to significant adverse events in children must be published in respected and widely read journals because of the great general interest today in vaccine safety. These journals can be expected to apply the highest standards of critical peer review to the results of any research that purports the existence of these associations and claims of causality.

1. Geier MR, Geier DA. Thimerosal in childhood vaccines, neurodevelopment disorders and heart disease in the United States. *J Am Physicians Surg.* 2003;8:6-11
2. Institute of Medicine, Immunization Safety Review Committee. *Immunization Safety Review: Thimerosal-Containing Vaccines and Neurodevelopmental Disorders*. Stratton K, Gable A, McCormick M, eds. Washington, DC: National Academies Press; 2001
3. Nelson KB, Bauman ML. Thimerosal and autism? *Pediatrics.* 2003;111:674-679